PCT

INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 : C07D 473/00 — A2

(11) International Publication Number: WO 95/28402

(43) International Publication Date: 26 October 1995 (26.10.95)

(21) International Application Number: PCT/EP95/01840

(22) International Filing Date: 19 April 1995 (19.04.95)

(30) Priority Data:
9407698.1 19 April 1994 (19.04.94) GB

(71) Applicant *(for all designated States except US)*: SMITHKLINE BEECHAM PLC [GB/GB]; New Horizons Court, Brentford, Middlesex TW8 9EP (GB).

(72) Inventor; and

(75) Inventor/Applicant *(for US only)*: DALES, John, Robert, Mansfield [GB/GB]; SmithKline Beecham Pharmaceuticals, Clarendon Road, Worthing, West Sussex BN14 8QH (GB).

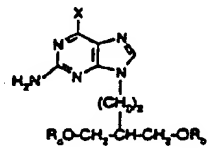
(74) Agent: TOCHER, Pauline; SmithKline Beecham, Corporate Intellectual Property, SB House, Great West Road, Brentford, Middlesex TW8 9BD (GB).

(81) Designated States: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT, UA, UG, US, UZ, VN, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG), ARIPO patent (KE, MW, SD, SZ, UG).

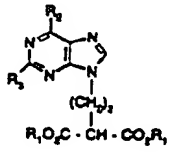
**Published**

*Without international search report and to be republished upon receipt of that report.*

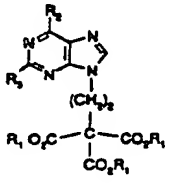
(54) Title: PREPARATION OF PURINES



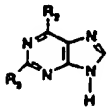
(A)



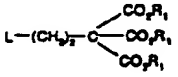
(I)



(VI)



(II)



(V)

(57) Abstract

A process for the preparation of a compound of formula (A) wherein: X is hydrogen, hydroxy, chloro, $C_{1-6}$ alkoxy or phenyl $C_{1-6}$ alkoxy; and $R_a$ and $R_b$ are hydrogen, or acyl or phosphate derivatives thereof, which process comprises: (i) the preparation of a compound of formula (I) whereiff $R_1$ is $C_{1-6}$ alkyl, or phenyl $C_{1-6}$ alkyl in which the phenyl group is optionally substituted; $R_2$ is hydrogen, hydroxy, chlorine, $C_{1-6}$ alkoxy, phenyl $C_{1-6}$ alkoxy or amino; and $R_3$ is halogen, $C_{1-6}$ alkylthio, $C_{1-6}$ alkylsulphonyl, azido, an amino group or a protected amino group, which preparation comprises the reaction of a compound of formula (II), wherein $R_2$ and $R_3$ are as defined for formula (I) with a compound of formula (V) wherein L is a leaving group and $R_1$ is as defined for formula (I), to give a compound of formula (VI), and thereafter converting the intermediate compound of formula (VI) to a compound of formula (I) via decarboxylation, and, as necessary or desired, interconverting variables $R_1$, $R_2$ and $R_3$ to further values of $R_1$, $R_2$ and $R_3$; (ii) the conversion of the resulting compound of formula (I) to a compound of formula (A) by converting variable $R_3$, when other than amino, to amino, reducing the ester groups $CO_2R_1$ to $CH_2OH$ and optionally forming acyl or phosphate derivatives thereof, and as necessary or desired converting variable $R_2$ in the compound of formula (I) to variable X in the compound of formula (A); characterised in that $R_2$ is chloro in formula (I).